

Attorney Docket No.: **BIS-043 (BI-0004US)**  
Inventor: **Simons and Gao**  
Serial No.: **09/276,868**  
Filing Date: **March 26, 1999**  
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**Amendments to the Specification:**

Please replace the paragraph beginning at page 7, line 5, with following rewritten paragraph:

--Figs. 1A-1D are presentations of empirical data showing the direct interaction between PR-39 peptide and the  $\alpha 7$  subunit of proteasomes intracellularly, wherein Fig. 1A recites the amino acid sequence of cloned mouse  $\alpha 7$  subunit (SEQ ID NO:7) and Fig. 1B shows the sequence alignment of C-terminal tails of mouse  $\alpha$  subunits  $\alpha 1$  (SEQ ID NO:8),  $\alpha 2$ ,  $\alpha 3$  (SEQ ID NO:9),  $\alpha 4$  (SEQ ID NO:10),  $\alpha 5$ ,  $\alpha 6$  (SEQ ID NO:11), and  $\alpha 7$  (SEQ ID NO:12);--

Please replace the paragraph beginning at page 23, line 15, with following rewritten paragraph:

--As conventionally known and reported [see for example, U.S. Patent No. 5,654,273], the specific peptide can be substituted using conservative substitutions of amino acids having the same or functionally equivalent charge and structure, except for the required amino acid sequence "Arg-Arg-Arg" at the N-terminus and the intermediate amino acid sequences "Pro-Pro-X-X-Pro-Pro-X-X-Pro" (SEQ ID NO:2) and "Pro-Pro-X-X-X-Pro-Pro-X-X-Pro" (SEQ ID NO:3) where X can be substituted freely using any amino acid. Thus, all of the preferred substituted amino acid sequences are of about the same size and each differ from the native PR-39 peptide sequence only by substitutions in the intermediate portions of the structure.--

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Please replace the paragraph beginning at page 25, line 1, with following rewritten paragraph:

--Merely as illustrative examples and preferred embodiments of the broad membership constituting this PR-39 derived oligopeptide family, the members comprising 15, 11 and 8 amino acid residues respectively in length are presented below as the PR15, PR11, and PR8 entities respectively. For comparison purposes only, the complete amino acid sequence of the native PR-39 peptide is presented as well.

PR-39:       1   2   3   4   5   6   7   8   9   10 11 12  
          Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg-Pro-  
  
          13 14 15 16 17 18 19 20 21 22 23 24  
          Arg-Pro-Pro-Pro-Phe-Phe-Pro-Pro-Arg-Leu-Pro-Pro-  
  
          25 26 27 28 29 30 31 32 33 34 35 36  
          Arg-Ile-Pro-Pro-Gly-Phe-Pro-Pro-Arg-Phe-Pro-Pro-  
  
          37 38 39  
          Arg-Phe-Pro ~~(SEQ ID NO:2)~~ (SEQ ID NO:1)

PR-15:       1   2   3   4   5   6   7   8   9   10 11 12  
          Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg-Pro-  
  
          13 14 15  
          Arg-Pro-Pro ~~(SEQ ID NO:3)~~ (SEQ ID NO:4)

PR-11:       1   2   3   4   5   6   7   8   9   10 11  
          Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg   ~~(SEQ ID~~  
          NO:4) (SEQ ID NO:5)

PR-8:        1   2   3   4   5   6   7   8  
          Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr ~~(SEQ ID NO:5)~~ (SEQ ID  
          NO:6)--

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Please replace the paragraph beginning at page 45, line 2, with following rewritten paragraph:

--To demonstrate the efficiency of shorter-length peptides which collectively are members of the PR-39 derived oligopeptide family in stimulating angiogenesis in-vivo, a novel peptide, PR11, composed of the first 11 amino acid residues [N-terminal end] of the native PR-39 sequence was purposely synthesized. The amino acid sequence of PR11 is as follows:

1	2	3	4	5	6	7	8	9	10	11
Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg <del>(SEQ ID NO:7)</del>										
<u>(SEQ ID NO:5)</u> .--										